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            annotation updated: Jul 15, 1999.
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KEYWORDS    Hydrolase; Glycosidase; 3D-structure.
SOURCE      Escherichia coli.
  ORGANISM  Escherichia coli
            Bacteria; Proteobacteria; gamma subdivision; Enterobacteriaceae;
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REFERENCE   1  (residues 1 to 1024)
  AUTHORS   Kalnins,A., Otto,K., Ruther,U. and Muller-Hill,B.
  TITLE     Sequence of the lacZ gene of Escherichia coli
  JOURNAL   EMBO J. 2 (4), 593-597 (1983)
  MEDLINE   84028567
  REMARK    SEQUENCE FROM N.A.
REFERENCE   2  (residues 1 to 1024)
  AUTHORS   BLATTNER,F.R., PLUNKETT,G.I.I.I., BLOCH,C.A., PERNA,N.T.,
            BURLAND,V., RILEY,M., COLLADO-VIDES,J., GLASNER,F.D., RODE,C.K.,
            MAYHEW,G.F., GREGOR,J., DAVIS,N.W., KIRKPATRICK,H.A., GOEDEN,M.A.,
            ROSE,D.J., MAU,B. and SHAO,Y.
  TITLE     The complete genome sequence of Escherichia coli K-12
  JOURNAL   Science 277 (5331), 1453-1474 (1997)
  MEDLINE   97426617
  REMARK    SEQUENCE FROM N.A.
            STRAIN=K12 / MG1655
REFERENCE   3  (residues 1 to 1024)
  AUTHORS   DUNCAN,M., ALLEN,E., ARAUJO,R., APARICIO,A.M., CHUNG,E., DAVIS,K.,
            FEDERSPIEL,N., HYMAN,R., KALMAN,S., KOMP,C., KURDI,O., LEW,H.,
            LIN,D., NAMATH,A., OEFNER,P., ROBERTS,D., SCHRAMM,S. and DAVIS,R.W.
  TITLE     Direct Submission
  JOURNAL   Submitted (??-NOV-1996) to the EMBL/GenBank/DDBJ databases
  REMARK    SEQUENCE FROM N.A.
REFERENCE   4  (residues 1 to 1024)
  AUTHORS   Fowler,A.V. and Zabin,I.
  TITLE     Amino acid sequence of beta-galactosidase. XI. Peptide ordering
            procedures and the complete sequence
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  JOURNAL   J. Biol. Chem. 253 (15), 5521-5525 (1978)
  MEDLINE   78218239
  REMARK    SEQUENCE.
REFERENCE   5  (residues 1 to 1024)
  AUTHORS   Calos,M.P. and Miller,J.H.
  TITLE     Molecular consequences of deletion formation mediated by the
            transposon Tn9
  JOURNAL   Nature 285 (5759), 38-41 (1980)
  MEDLINE   80188189
  REMARK    SEQUENCE OF 355-475 FROM N.A.
REFERENCE   6  (residues 1 to 1024)
  AUTHORS   Buchel,D.E., Gronenborn,B. and Muller-Hill,B.
  TITLE     Sequence of the lactose permease gene
  JOURNAL   Nature 283 (5747), 541-545 (1980)
  MEDLINE   80120651
  REMARK    SEQUENCE OF 1007-1023 FROM N.A.
REFERENCE   7  (residues 1 to 1024)
  AUTHORS   Fowler,A.V. and Smith,P.J.
  TITLE     The active site regions of lacZ and ebg beta-galactosidases are
            homologous
  JOURNAL   J. Biol. Chem. 258 (17), 10204-10207 (1983)
  MEDLINE   83290932
  REMARK    ACTIVE SITE REGIONS.
REFERENCE   8  (residues 1 to 1024)
  AUTHORS   Herrchen,M. and Legler,G.
  TITLE     Identification of an essential carboxylate group at the active site
            of lacZ beta-galactosidase from Escherichia coli
  JOURNAL   Eur. J. Biochem. 138 (3), 527-531 (1984)
  MEDLINE   84108409
  REMARK    ACTIVE SITE GLU-461.
REFERENCE   9  (residues 1 to 1024)
  AUTHORS   Gebler,J.C., Aebersold,R. and Withers,S.G.
  TITLE     Glu-537, not Glu-461, is the nucleophile in the active site of (lac
            Z) beta-galactosidase from Escherichia coli
  JOURNAL   J. Biol. Chem. 267 (16), 11126-11130 (1992)
  MEDLINE   92283812
  REMARK    ACTIVE SITE GLU-537.
REFERENCE   10 (residues 1 to 1024)
  AUTHORS   Jacobson,R.H., Zhang,X.J., DuBose,R.F. and Matthews,B.W.
  TITLE     Three-dimensional structure of beta-galactosidase from E. coli
  JOURNAL   Nature 369 (6483), 761-766 (1994)
  MEDLINE   94277211
  REMARK    X-RAY CRYSTALLOGRAPHY (3.5 ANGSTROMS).
COMMENT     ---------------------------------------------------------------
            This SWISS-PROT entry is copyright. It is produced through a
            collaboration between the Swiss Institute of Bioinformatics and
            the EMBL outstation - the European Bioinformatics Institute.
            The original entry is available from http://www.expasy.ch/sprot
            and http://www.ebi.ac.uk/sprot
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            BETA-D-GALACTOSE RESIDUES IN BETA-D-GALACTOSIDES.
            [SUBUNIT] HOMOTETRAMER.
            [SIMILARITY] BELONGS TO FAMILY 2 OF GLYCOSYL HYDROLASES.
            [DATABASE] NAME=Worthington enzyme manual;
            WWW='http://www.worthington-biochem.com/manual/G/BG.html'.
            [DATABASE] NAME=ProZyme technical fact sheet;
            WWW='http://www.prozyme.com/technical/bgaldata.html'.
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      121 tgcysltfnv deswlqegqt riifdgvnsa fhlwcngrwv gygqdsrlps efdlsaflra
      181 genrlavmvl rwsdgsyled qdmwrmsgif rdvsllhkpt tqisdfhvat rfnddfsrav
      241 leaevqmcge lrdylrvtvs lwqgetqvas gtapfggeii derggyadrv tlrlnvenpk
      301 lwsaeipnly ravvelhtad gtlieaeacd vgfrevrien gllllngkpl lirgvnrheh
      361 hplhgqvmde qtmvqdillm kqnnfnavrc shypnhplwy tlcdryglyv vdeanietha
      421 mvpmnrltdd prwlpamser vtrmvqrdrn hpsviiwslg nesghganhd alyrwiksvd
      481 psrpvqyegg gadttatdii cpmyarvded qpfpavpkws ikkwlslpge trplilceya
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     1021 wcqk
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102(a) date

L12 ANSWER 1 OF 6 BIOSIS COPYRIGHT 2000 BIOSIS
AN 2000:148109 BIOSIS
DN PREV200000148109
TI Isolation of neuronal precursor cells by **FACS** from the Talpha1-**GFP transgenic** animals.
AU Sawamoto, K. (1); Ogawa, Y. (1); Saiwaki, T. (1); Kawaguchi, A. (1); Miyata, T. (1); Goldman, S. A.; Okano, H.
CS (1) Dept. of Neuroanatomy, Biomed. Res. Ctr., Osaka Univ. Med. Sch., Suita, Osaka, 565-0871 Japan
SO Society for Neuroscience Abstracts., (1999) Vol. 25, No. 1-2, pp. 2043. Meeting Info.: 29th Annual Meeting of the Society for Neuroscience. Miami Beach, Florida, USA October 23-28, 1999 Society for Neuroscience . ISSN: 0190-5295.
DT Conference
LA English
SL English

L2 ANSWER 9 OF 10 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1998:528162 BIOSIS
DN PREV199800528162
TI Visualization of neuronal stem cells in vivo.
AU Yamaguchi, Masahiro (1); Suzuki, Misao; Mori, Kensaku
CS (1) PRESTO, Japan Sci. Technol. Corp., Soraku-gu, Kyoto 619-0237 Japan
SO Neuroscience Research Supplement, (1998) No. 22, pp. S286.
Meeting Info.: 21st Annual Meeting of the Japan Neuroscience Society and the First Joint Meeting of the Japan Neuroscience Society and the Japanese Society for Neurochemistry Tokyo, Japan September 21-23, 1998 Japan Neuroscience Society
. ISSN: 0921-8696.
DT Conference
LA English

L8 ANSWER 2 OF 2 MEDLINE
AN 97388554 MEDLINE
DN 97388554
TI Brief expression of a GFP cre fusion gene in embryonic stem cells allows rapid retrieval of site-specific genomic deletions.
AU Gagneten S; Le Y; Miller J; Sauer B
CS Laboratory of Biochemistry and Metabolism, National Institute of Diabetes, Digestive and Kidney Disease, National Institutes of Health, Bethesda, MD 20892-1800, USA.
SO NUCLEIC ACIDS RESEARCH, (1997 Aug 15) 25 (16) 3326-31.
Journal code: O8L. ISSN: 0305-1048.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199711
EW 19971103
AB The Cre DNA recombinase of bacteriophage P1 has become a useful tool for precise genomic manipulation in embryonic stem (ES) cells that have been gene modified by homologous recombination. We have re-engineered the cre gene to allow ready identification of living Cre+cells by constructing a functional fusion between Cre and an enhanced **green** fluorescent protein from Aequorea victoria (GFPS65T). The GFP cre fusion gene product rapidly targeted the nucleus in the absence of any exogenous nuclear localization signal. Moreover, GFPCre catalyzed efficient DNA recombination in both a mouse 3T3 derivative cell line and in murine ES cells. Fluorescence- activated cell sorting (**FACS**) of transiently GFP cre -transfected ES cells not only allowed rapid and efficient isolation of Cre+cells after DNA transfection but also demonstrated that a burst of Cre expression is sufficient to commit cells to Cre-mediated 'pop-out' of loxP -tagged DNA from the genome. Thus, GFP cre allows rapid identification of living cells in which loxP - flanked DNA sequences are destined to be removed from the genome by Cre-mediated recombination without reliance on recombinational activation or inactivation of a marker gene at the target locus. In addition, the GFP cre fusion gene will prove useful in tracing tissue-specific Cre expression in **transgenic** animals, thereby facilitating the generation and analysis of conditional gene knockout mice.

41, 24, 13

NESTIN PROMOTER - TRANSGENICS

L2 ANSWER 36 OF 37 MEDLINE
AN 94121904 MEDLINE
DN 94121904
TI Independent regulatory elements in the **nestin** gene direct **transgene** expression to neural stem cells or muscle precursors [published erratum appears in Neuron 1994 Jun;12(6):following 1388].
AU Zimmerman L; Parr B; Lendahl U; Cunningham M; McKay R; Gavin B; Mann J; Vassileva G; McMahon A
CS Department of Brain and Cognitive Sciences, Massachusetts Institute of Technology, Cambridge 02139..
SO NEURON, (1994 Jan) 12 (1) 11-24.
Journal code: AN8. ISSN: 0896-6273.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199405
AB Changes in intermediate filament gene expression occur at key steps in the differentiation of cell types in the mammalian CNS. Neuroepithelial stem cells express the intermediate filament protein **nestin** and down-regulate it sharply at the transition from proliferating stem cell to postmitotic neuron. **Nestin** is also expressed in muscle precursors but not in mature muscle cells. We show here that in **transgenic** mice, independent cell type-specific elements in the first and second introns of the **nestin** gene consistently direct reporter gene expression to developing muscle and neural precursors, respectively. The second intron contains an enhancer that functions in CNS stem cells, suggesting that there may be a single transcriptional mechanism regulating the CNS stem cell state. This enhancer is much less active in the PNS. The identification of these elements facilitates analysis of mechanisms controlling the switch in gene expression that occurs when muscle and brain precursors terminally differentiate.

→ Ex of ot of claimed cells

QP 356.2 N48

What promoter??
Nestin Rat

L2 ANSWER 33 OF 37 MEDLINE
AN 96017714 MEDLINE
DN 96017714
TI Rapid, widespread, and longlasting induction of **nestin** contributes to the generation of glial scar tissue after CNS injury.
AU Frisen J; Johansson C B; Torok C; Risling M; Lendahl U
CS Department of Neuroscience, Karolinska Institute, Stockholm, Sweden..
SO JOURNAL OF CELL BIOLOGY, (1995 Oct) 131 (2) 453-64.
Journal code: HMV. ISSN: 0021-9525.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199602
AB Neuronal regeneration does generally not occur in the central nervous system (CNS) after injury, which has been attributed to the generation of glial scar tissue. In this report we show that the composition of the glial scar after traumatic CNS injury in rat and mouse is more complex than previously assumed: expression of the intermediate filament **nestin** is induced in reactive astrocytes. **Nestin** induction occurs within 48 hours in the spinal cord both at the site of lesion and in degenerating tracts and lasts for at least 13 months. **Nestin** expression is induced with similar kinetics in the crushed optic nerve. In addition to the expression in reactive astrocytes, we also observed **nestin** induction within 48 hours after injury in cells close to the central canal in the spinal cord, while **nestin** expressing cells at later timepoints were found progressively further out from the central canal. This dynamic pattern of **nestin** induction after injury was mimicked by lacZ expressing cells in **nestin** promoter/lacZ **transgenic** mice, suggesting that defined **nestin** regulatory regions mediate the injury response. We discuss the possibility that the spatiotemporal pattern of **nestin** expression reflects a population of **nestin** positive cells, which proliferates and migrates from a region close to the central canal to the site of lesion in response to injury.

Enhancer ?

L2 ANSWER 30 OF 37 MEDLINE
AN 97147786 MEDLINE
DN 97147786
TI Bypass of lethality with mosaic mice generated by Cre-loxP-mediated recombination.
AU Betz U A; Vosshenrich C A; Rajewsky K; Muller W
CS Institute for Genetics, University of Cologne, Germany..
ubetz@mac.genetik.uni-koeln.de
SO CURRENT BIOLOGY, (1996 Oct 1) 6 (10) 1307-16.
Journal code: B44. ISSN: 0960-9822.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199704
EW 19970403
AB BACKGROUND: The analysis of gene function based on the generation of mutant mice by homologous recombination in embryonic stem cells is limited if gene disruption results in embryonic lethality. Mosaic mice, which contain a certain proportion of mutant cells in all organs, allow lethality to be circumvented and the potential of mutant cells to contribute to different cell lineages to be analyzed. To generate mosaic animals, we used the bacteriophage P1-derived Cre-loxP recombination system, which allows gene alteration by Cre-mediated deletion of loxP-flanked gene segments. RESULTS: We generated **nestin**-cre **transgenic** mouse lines, which expressed the Cre recombinase under the control of the rat **nestin** promoter and its second intron enhancer. In crosses to animals carrying a loxP-flanked target gene, partial deletion of the loxP-flanked allele occurred before day 10.5 post coitum and was detectable in all adult organs examined, including germ-line cells. Using this approach, we generated mosaic mice containing cells deficient in the gamma-chain of the interleukin-2 receptor (IL-2R gamma); in these animals, the IL-2R gamma-deficient cells were underrepresented in the thymus and spleen. Because mice deficient in DNA polymerase beta die perinatally, we studied the effects of DNA polymerase beta deficiency in mosaic animals. We found that some of the mosaic polymerase beta-deficient animals were viable, but were often reduced in size and weight. The fraction of DNA polymerase beta-deficient cells in mosaic embryos decreased during embryonic development, presumably because wild-type cells had a competitive advantage. CONCLUSIONS: The **nestin**-cre **transgenic** mice can be used to generate mosaic animals in which target genes are mutated by Cre-mediated recombination of loxP-flanked target genes. By using mosaic animals, embryonic lethality can be bypassed and cell lineages for whose development a given target gene is critical can be identified. In the case of DNA polymerase beta, deficient cells are already selected against during embryonic development, demonstrating the general importance of this protein in multiple cell types.

is cre fluorescent?

L2 ANSWER 29 OF 37 MEDLINE
AN 97258113 MEDLINE
DN 97258113
TI An evolutionarily conserved region in the second intron of the human **nestin** gene directs gene expression to CNS progenitor cells and to early neural crest cells.
AU Lothian C; Lendahl U
CS Department of Cell and Molecular Biology, Medical Nobel Institute, Karolinska Institute, Stockholm, Sweden.
SO EUROPEAN JOURNAL OF NEUROSCIENCE, (1997 Mar) 9 (3) 452-62.
Journal code: BYG. ISSN: 0953-816X.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199709
EW 19970901
AB Central nervous system (CNS) progenitor cells transiently proliferate in the embryonic neural tube and give rise to neurons and glial cells. A characteristic feature of the CNS progenitor cells is expression of the intermediate filament **nestin** and it was previously shown that the rat **nestin** second intron functions as an enhancer, directing gene expression to CNS progenitor cells. In this report we characterize the **nestin** enhancer in further detail. Cloning and sequence analysis of the rat and human **nestin** second introns revealed local domains of high sequence similarity in the 3' portion of the introns. **Transgenic** mice were generated with the most conserved 714 bp in the 3' portion of the intron, or with the complete, 1852 bp, human second intron, coupled to the reporter gene lacZ. The two constructs gave a very similar **nestin**-like expression pattern, indicating that the important control elements reside in the 714 bp element. Expression was observed starting in embryonic day (E)7.5 neural plate, and at E10.5 CNS progenitor cells throughout the neural tube expressed lacZ. At E12.5, lacZ expression was more restricted and confined to proliferating regions in the neural tube. An interesting difference, compared to the rat **nestin** second intron, was that the human intron at E10.5 mediated lacZ expression also in early migrating neural crest cells, which is a site of endogenous **nestin** expression. In conclusion, these data show that a relatively short, evolutionarily conserved region is sufficient to control gene expression in CNS progenitor cells, but that the same region differs between rodents and primates in its capacity to control expression in neural crest cells.

promotor?

L2 ANSWER 28 OF 37 MEDLINE
AN 97359974 MEDLINE
DN 97359974
TI Limb proprioceptive deficits without neuronal loss in **transgenic** mice overexpressing neurotrophin-3 in the developing nervous system.
AU Ringstedt T; Kucera J; Lendahl U; Ernfors P; Ibanez C F
CS Department of Neuroscience, Karolinska Institute, Stockholm, Sweden.
SO DEVELOPMENT, (1997 Jul) 124 (13) 2603-13.
Journal code: ECW. ISSN: 0950-1991.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199710
AB The role of neurotrophin-3 (NT3) during sensory neuron development was investigated in **transgenic** mice overexpressing NT3 under the control of the promoter and enhancer regions of the **nestin** gene, an intermediate filament gene widely expressed in the developing nervous system. Most of these mice died during the first postnatal day, and all showed severe limb ataxia suggestive of limb proprioceptive dysfunction. Tracing and histological analyses revealed a complete loss of spindles in limb muscles, absence of peripheral and central Ia projections, and lack of cells immunoreactive to parvalbumin in the dorsal root ganglion (DRG). Despite these deficits, there was no neuronal loss in the DRG of these mice. At birth, **transgenic** DRG showed increased neuron numbers, and displayed a normal proportion of neurons expressing substance P, calcitonin gene-related peptide and the NT3 receptor trkC. **Transgenic** dorsal roots exhibited an increased number of axons at birth, indicating that all sensory neurons in **transgenic** mice projected to the dorsal spinal cord. Despite the absence of central Ia afferents reaching motorneurons, several sensory fibers were seen projecting towards ectopic high levels of NT3 in the midline of **transgenic** spinal cords. These findings suggest novel roles for NT3 in differentiation of proprioceptive neurons, target invasion and formation of Ia projections which are independent from its effects on neuronal survival.

102(b) NT3 hms 4W
11y
out of 258 cms

L2 ANSWER 27 OF 37 MEDLINE
AN 97391813 MEDLINE
DN 97391813
TI **Transgenic** analysis of central nervous system development and regeneration.
AU Lendahl U
CS Department of Cell and Molecular Biology, Medical Nobel Institute, Karolinska Institute, Stockholm, Sweden.
SO ACTA ANAESTHESIOLOGICA SCANDINAVICA. SUPPLEMENTUM, (1997) 110 116-8. Journal code: 08Q. ISSN: 0515-2720.
CY Denmark
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199711
EW 19971103
AB The **transgenic** technique allows specific genetic alterations to be made in all cells of an animal and this has greatly improved our understanding of how the embryonic and adult central nervous system (CNS) develop. The CNS originates from the neuroectoderm in the neural plate on the dorsal side of the embryo and after closure of the neural tube the cells of the neuroepithelium, i.e. the CNS stem cells, transiently proliferate to generate neurons and glial cells. Here we review our attempts to gain insights into the control of CNS development. We have identified a gene, **nestin**, which is predominantly expressed in embryonic and adult CNS stem cells. In addition to its normal expression in the CNS stem cells, **nestin** is reexpressed in CNS tumors and in the adult spinal cord and brain after CNS injury. By using the lacZ reporter gene assay in **transgenic** mice, we have identified regulatory regions (enhancer) in the **nestin** gene required for expression in embryonic CNS stem cells and in the adult spinal cord after injury. In a second project, we have cloned and characterized the Notch gene family (the Notch 1, 2 and 3 genes) in mouse and man. These genes encode trans-membrane receptors, which appear to be key regulatory molecules for proliferation and differentiation both in the developing CNS and in other tissues. Expression of an activated form of the Notch 3 receptor from the **nestin** promoter in **transgenic** mice leads to a lethal, exencephaly-like phenotype in the embryo, probably as a result of excess proliferation of the CNS stem cells. The recent finding that the Notch 3 gene is the genetic cause for familial stroke is discussed in the context of current models for Notch function.

L2 ANSWER 13 OF 37 MEDLINE
AN 1999117355 MEDLINE
DN 99117355
TI Heterogeneity of neural progenitor cells revealed by enhancers in the **nestin** gene.
AU Yaworsky P J; Kappen C
CS Molecular Neuroscience Program, Samuel C. Johnson Medical Research Center, Scottsdale, Arizona, 85259, USA.
SO DEVELOPMENTAL BIOLOGY, (1999 Jan 15) 205 (2) 309-21.
Journal code: E7T. ISSN: 0012-1606.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199904
EW 19990404
AB Using **transgenic** embryos, we have identified two distinct CNS progenitor cell-specific enhancers, each requiring the cooperation of at least two independent regulatory sites, within the second intron of the rat **nestin** gene. One enhancer is active throughout the developing CNS, while the other is specifically active in the ventral midbrain. These experiments demonstrate that neural progenitor cells in the midbrain constitute a unique subpopulation based upon their ability to activate the midbrain regulatory element. Our finding of differential enhancer activity from a gene encoding a structural protein reveals a previously unrecognized diversity in neural progenitor cell populations.